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on 12-11-01
By: Nancy Ramos
Printed: NANCY RAMOS

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Bandman, et al.

Title: RNA METABOLISM PROTEINS

PCT Serial No.: PCT/US00/16644 International Filing Date: 15 June 2000

Examiner: To Be Assigned Group Art Unit: To Be Assigned

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Commissioner for Patents
**BOX PATENT APPLICATION**
Washington, D.C. 20231

**REQUEST TO PUBLISH APPLICATION WITH ARTICLE 34 AMENDMENTS**

Sir:

Applicants respectfully request that the present application be published under 35 U.S.C. § 122(b) with the claims as amended under PCT Article 34 on the attached substitute sheets, and which are submitted with the attached PCT application, rather than as originally filed.

Applicants submit that the Article 34 amendments should be considered as a part of the application as filed, as they were submitted in the form of replacement sheets during Chapter II examination of the PCT application, and should not be considered as a preliminary amendment which cannot be published unless submitted in electronic form.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108. This form is enclosed in duplicate.**

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 11 Dec 2001

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## CHAPTER II

INTERNATIONAL EXAMINING AUTHORITY (IPEA/US)

| PCT/US00/16644 | 15 June 2000 | 17 June 1999 |
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RNA METABOLISM PROTEINS

TITLE OF INVENTION

INCYTE GENOMICS, INC.

APPLICANT

**United States Patent and Trademark Office**
**P.O. Box PCT**
**Washington, D.C. 20231**

## ARTICLE 34 AMENDMENT

Dear Sirs:

Please add new claims 28-90 in the above referenced international application as indicated below. A clean copy of the claims is attached (see pages 79/1-79/8). The replacement pages

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting antagonist activity in the sample.

23. A pharmaceutical composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.

24. A method for treating a disease or condition associated with overexpression of functional RMEP, comprising administering to a patient in need of such treatment a pharmaceutical composition of claim 23.

25. A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:

a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:

a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,

b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, and

b) detecting altered expression of the target polynucleotide.

28. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

29. A method for assessing toxicity of a test compound, said method comprising:

a) treating a biological sample containing nucleic acids with the test compound;

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

c) quantifying the amount of hybridization complex; and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

30. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:1.

31. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:2.

32. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:3.

33. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:4.

34. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:6.

35. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:7.

36. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:8.

37. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:9.

38. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:10.

39. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:11.

40. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:12.

41. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:13.

42. A diagnostic test for a condition or disease associated with the expression of human RNA metabolism proteins (RMEP) in a biological sample comprising the steps of:

a) combining the biological sample with an antibody of claim 10, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex; and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

43. The antibody of claim 10, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a $F(ab')_2$ fragment, or

e) a humanized antibody.

44. A composition comprising an antibody of claim 10 and an acceptable excipient.

45. A method of diagnosing a condition or disease associated with the expression of human RNA metabolism proteins (RMEP) in a subject, comprising administering to said subject an effective amount of the composition of claim 44.

46. A composition of claim 44, wherein the antibody is labeled.

47. A method of diagnosing a condition or disease associated with the expression of human RNA metabolism proteins (RMEP) in a subject, comprising administering to said subject an effective amount of the composition of claim 46.

48. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 10 comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibodies from said animal; and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13.

49. An antibody produced by a method of claim 48.

50. A composition comprising the antibody of claim 49 and a suitable carrier.

51. A method of making a monoclonal antibody with the specificity of the antibody of claim 10 comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibody producing cells from the animal;

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;

d) culturing the hybridoma cells; and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13.

52. A monoclonal antibody produced by a method of claim 51.

53. A composition comprising the antibody of claim 52 and a suitable carrier.

54. The antibody of claim 10, wherein the antibody is produced by screening a Fab expression library.

55. The antibody of claim 10, wherein the antibody is produced by screening a recombinant immunoglobulin library.

56. A method for detecting a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 in a sample, comprising the steps of:

a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 in the sample.

57. A method of purifying a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 from a sample, the method comprising:

a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) separating the antibody from the sample and obtaining the purified polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13.

58. A microarray wherein at least one element of the microarray is a polynucleotide of claim 12.

59. A method for generating a transcript image of a sample which contains polynucleotides, the method comprising the steps of:

a) labeling the polynucleotides of the sample,

b) contacting the elements of the microarray of claim 58 with the labeled polynucleotides of the sample under conditions suitable for the formation of a hybridization complex, and

c) quantifying the expression of the polynucleotides in the sample.

60. An array comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, wherein at least one of said nucleotide molecules comprises a first oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, said target polynucleotide having a sequence of claim 11.

61. An array of claim 60, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

62. An array of claim 60, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 60 contiguous nucleotides of said target polynucleotide.

63. An array of claim 60, which is a microarray.

64. An array of claim 60, further comprising said target polynucleotide hybridized to said first oligonucleotide or polynucleotide.

65. An array of claim 60, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

66. An array of claim 60, wherein each distinct physical location on the substrate contains multiple nucleotide molecules having the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another physical location on the substrate.

67. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:1.

68. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2.

69. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:3.

70. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:4.

71. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:6.

72. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:7.

73. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:8.

74. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:9.

75. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:10.

76. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:11.

77. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:12.

78. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:13.

79. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:14.

80. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:15.

81. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:16.

82. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:17.

83. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:19.

84. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:20.

85. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:21.

86. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:22.

87. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:23.

88. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:24.

89. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:25.

90. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:26.